

Amendments to the Specification:

The paragraph beginning at page 124, line 27, has been amended as follows:

Percent amino acid sequence identity may also be determined using the sequence comparison program NCBI-BLAST2 (Altschul et al., Nucleic Acids Res. 25:3389-3402 (1997)).
~~The NCBI BLAST2 sequence comparison program may be downloaded from~~
~~<http://www.ncbi.nlm.nih.gov>.~~ NCBI-BLAST2 uses several search parameters, wherein all of those search parameters are set to default values including, for example, unmask = yes, strand = all, expected occurrences = 10, minimum low complexity length = 15/5, multi-pass e-value = 0.01, constant for multi-pass = 25, dropoff for final gapped alignment = 25 and scoring matrix = BLOSUM62.

The paragraph beginning at page 127, line 10, has been amended as follows:

Percent nucleic acid sequence identity may also be determined using the sequence comparison program NCBI-BLAST2 (Altschul et al., Nucleic Acids Res. 25:3389-3402 (1997)).
~~The NCBI BLAST2 sequence comparison program may be downloaded from~~
~~<http://www.ncbi.nlm.nih.gov>.~~ NCBI-BLAST2 uses several search parameters, wherein all of those search parameters are set to default values including, for example, unmask = yes, strand = all, expected occurrences = 10, minimum low complexity length = 15/5, multi-pass e-value = 0.01, constant for multi-pass = 25, dropoff for final gapped alignment = 25 and scoring matrix = BLOSUM62.

The paragraph beginning at page 237, line 2, has been amended as follows:

A cDNA sequence isolated in the amylase screen as described in Example 2 above was found, by BLAST and FastA sequence alignment, to have sequence homology to a nucleotide sequence encoding sarcoma-associated protein SAS. This cDNA sequence is herein designated DNA23020 (see Figure 16). The DNA23020 sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ™, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altshul et al., Methods in Enzymology 266:460-480 (1996)). Those

comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington; <http://bozeman.mbt.washington.edu/phrap.does/phrap.html>). The consensus sequence obtained therefrom is herein designated DNA35858. Two proprietary Genentech ESTs were employed in the assembly wherein those EST sequences are herein identified as DNA21971 (Figure 17; SEQ ID NO:38) and DNA29037 (Figure 18; SEQ ID NO:39).

The paragraph beginning at page 278, line 26, has been amended as follows:

A cDNA sequence was isolated in the amylase screen described in Example 2 above and is herein designated DNA13199 (Figure 134; SEQ ID NO:332). The DNA13199 sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altshul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into consensus DNA sequences with the program "phrap" (Phil Green, University of Washington, Seattle, Washington; <http://bozeman.mbt.washington.edu/phrap.does/phrap.html>). The consensus sequence obtained therefrom is herein designated as DNA22778.

The paragraph beginning at page 279, line 26, has been amended as follows:

A cDNA sequence isolated in the amylase screen described in Example 2 above was herein designated DNA37642 (Figure 137, SEQ ID NO:338). The DNA37642 sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ™, Incyte Pharmaceuticals, Palo Alto, CA) to identify homologies therebetween. The homology search was performed using the computer program BLAST or BLAST2 (Altshul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into consensus DNA sequences with the program "phrap" (Phil Green, University of Washington,

Seattle, Washington; <http://bozeman.mbt.washington.edu/phrap.does/phrap.html>). The consensus sequence obtained is herein designated DNA48615.

The paragraph beginning at page 313, line 27, has been amended as follows:

A cDNA isolated in the amylase screen described in Example 2 above is herein designated DNA26832 (Figure 220; SEQ ID NO:516). The sequence of DNA26832 was then used to search expressed sequence tag (EST) databases. The EST databases included public EST databases (e.g., GenBank) and a proprietary EST database (LIFESEQ™, Incyte Pharmaceuticals, Palo Alto, CA). The search was performed using the computer program BLAST or BLAST2 (Altshul et al., *Methods in Enzymology* 266: 469-480 [1996]). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode proteins were clustered and assembled into consensus DNA sequences with the program "phrap" (Phil Green, University of Washington, Seattle, [Washington Washington;](http://bozeman.mbt.washington.edu/phrap.does/phrap.html) <http://bozeman.mbt.washington.edu/phrap.does/phrap.html>).

The paragraph beginning at page 315, line 20, has been amended as follows:

Human thrombopoietin (THPO) is a glycosylated hormone of 352 amino acids consisting of two domains. The N-terminal domain, sharing 50% similarity to erythropoietin, is responsible for the biological activity. The C-terminal region is required for secretion. The gene for thrombopoietin (THPO) maps to human chromosome 3q27-q28 where the six exons of this gene span 7 kilobase base pairs of genomic DNA (Chang et al., *Genomics* 26: 636-7 (1995); Foster et al., *Proc. Natl. Acad. Sci. USA* 91: 13023-7 (1994); Gurney et al., *Blood* 85: 981-988 (1995)). In order to determine whether there were any genes encoding THPO homologues located in close proximity to THPO, genomic DNA fragments from this region were identified and sequenced. Three P1 clones and one PAC clones (Genome Systems Inc., St. Louis, MO; cat. Nos. P1-2535 and PAC-6539) encompassing the THPO locus were isolated and a 140 kb region was sequenced using the ordered shotgun strategy (Chen et al., *Genomics* 17: 651-656 (1993)), coupled with a PCR-based gap filling approach. Analysis reveals that the region is gene-rich with four additional genes located very close to THPO: tumor necrosis factor-receptor type 1 associated protein 2 (TRAP2) and elongation initiation factor gamma (*eIF4f*) (*eIF4g*), chloride channel 2 (CLCN2) and RNA polymerase II subunit hRPB17. While no THPO homolog was

found in the region, four novel genes have been predicted by computer-assisted gene detection (GRAIL)(Xu et al., Gen. Engin. 16: 241-253 (1994), the presence of CpG islands (Cross, S. and Bird, A., Curr. Opin. Genet. & Devel. 5: 109-314 (1995), and homology to known genes (as detected by WU-BLAST2.0)(Altschul and Gish, Methods Enzymol. 266: 460-480 (1996) (<http://blast.wustl.edu/blast/README.html>).

The paragraph beginning at page 317, line 1, has been amended as follows:

~~ABI DYE-primer™ ABI DYE-primer™~~ chemistry (PE Applied Biosystems, Foster City, CA; Cat. No.: 402112) was used to end-sequence the lambda and plasmid subclones. ~~ABI DYE-terminator™ ABI DYE-terminator™~~ chemistry (PE Applied Biosystems, Foster City, CA, Cat. No: 403044) was used to sequence the PCR products with their respective PCR primers. The sequences were collected with an ABI377 instrument. For PCR products larger than 1kb, walking primers were used. The sequences of contigs generated by the OSS strategy in ~~AutoAssembler™ AutoAssembler™~~ (PE Applied Biosystems, Foster City, CA; Cat. No: 903227) and the gap-filling sequencing trace files were imported into ~~Sequencher™ Sequencher™~~ (Gene Codes Corp., Ann Arbor, MI) for overlapping and editing. The sequences generated by the total shotgun strategy were assembled using Phred and Phrap and edited using Consed (<http://chimera.biotech.washington.edu/uwgc/projects.htm>) and GFP (Genome Reconstruction Manager for Phrap), version 1.2 (<http://stork.cellb.bcm.tmc.edu/gfp/>).

The paragraph beginning at page 317, line 21, has been amended as follows:

The identification and characterization of coding regions was carried out as follows:

First, repetitive sequences were masked using RepeatMasker (A.F.A. Smit & P. Green; http://ftp.genome.washington.edu/RM/RM_details.html) which screens DNA sequences in FastA format against a library of repetitive elements and returns a masked query sequence. Repeats not masked were identified by comparing the sequence to the GenBank database using WUBLAST2.0 [Altschul, S & Gish, W., Methods Enzymol. 266: 460-480 (1996); <http://blast.wustl.edu/blast/README.html>] and were masked manually.



The paragraph beginning at page 376, line 34, has been amended as follows:

The following materials have been deposited with the American Type Culture Collection,

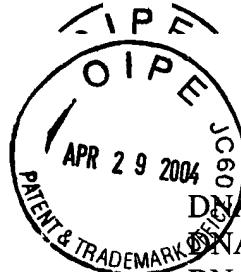
12301 Parklawn Drive, Rockville, MD, 10801 University Boulevard, Manassas,

VA 20110-2209, USA (ATCC):

| <u>Material</u> | <u>ATCC Dep. No.</u> | <u>Deposit Date</u> |
|-----------------|----------------------|---------------------|
| DNA39987-1184 | ATCC 209786 | April 21, 1998 |
| DNA40625-1189 | ATCC 209788 | April 21, 1998 |
| DNA23318-1211 | ATCC 209787 | April 21, 1998 |
| DNA39979-1213 | ATCC 209789 | April 21, 1998 |
| DNA40594-1233 | ATCC 209617 | February 5, 1998 |
| DNA45416-1251 | ATCC 209620 | February 5, 1998 |
| DNA45419-1252 | ATCC 209616 | February 5, 1998 |
| DNA52594-1270 | ATCC 209679 | March 17, 1998 |
| DNA45234-1277 | ATCC 209654 | March 5, 1998 |
| DNA49624-1279 | ATCC 209655 | March 5, 1998 |
| DNA48309-1280 | ATCC 209656 | March 5, 1998 |
| DNA46776-1284 | ATCC 209721 | March 31, 1998 |
| DNA50980-1286 | ATCC 209717 | March 31, 1998 |
| DNA50913-1287 | ATCC 209716 | March 31, 1998 |
| DNA50914-1289 | ATCC 209722 | March 31, 1998 |
| DNA48296-1292 | ATCC 209668 | March 11, 1998 |
| DNA32284-1307 | ATCC 209670 | March 11, 1998 |
| DNA36343-1310 | ATCC 209718 | March 31, 1998 |
| DNA40571-1315 | ATCC 209784 | April 21, 1998 |
| DNA41386-1316 | ATCC 209703 | March 26, 1998 |
| DNA44194-1317 | ATCC 209808 | April 28, 1998 |
| DNA45415-1318 | ATCC 209810 | April 28, 1998 |
| DNA44189-1322 | ATCC 209699 | March 26, 1998 |
| DNA48304-1323 | ATCC 209811 | April 28, 1998 |
| DNA49152-1324 | ATCC 209813 | April 28, 1998 |
| DNA49646-1327 | ATCC 209705 | March 26, 1998 |
| DNA49631-1328 | ATCC 209806 | April 28, 1998 |
| DNA49645-1347 | ATCC 209809 | April 28, 1998 |
| DNA45493-1349 | ATCC 209805 | April 28, 1998 |
| DNA48227-1350 | ATCC 209812 | April 28, 1998 |
| DNA41404-1352 | ATCC 209844 | May 6, 1998 |
| DNA44196-1353 | ATCC 209847 | May 6, 1998 |
| DNA52187-1354 | ATCC 209845 | May 6, 1998 |
| DNA48328-1355 | ATCC 209843 | May 6, 1998 |
| DNA56352-1358 | ATCC 209846 | May 6, 1998 |
| DNA53971-1359 | ATCC 209750 | April 7, 1998 |
| DNA50919-1361 | ATCC 209848 | May 6, 1998 |
| DNA44179-1362 | ATCC 209851 | May 6, 1998 |



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|-------------------|-------------|------------------|
| DNA54002-1367 | ATCC 209754 | April 7, 1998 |
| DNA53906-1368 | ATCC 209747 | April 7, 1998 |
| DNA52185-1370 | ATCC 209861 | May 14, 1998 |
| DNA53977-1371 | ATCC 209862 | May 14, 1998 |
| DNA57253-1382 | ATCC 209867 | May 14, 1998 |
| DNA58847-1383 | ATCC 209879 | May 20, 1998 |
| DNA58747-1384 | ATCC 209868 | May 14, 1998 |
| DNA57689-1385 | ATCC 209869 | May 14, 1998 |
| DNA23330-1390 | ATCC 209775 | April 14, 1998 |
| DNA26847-1395 | ATCC 209772 | April 14, 1998 |
| DNA53974-1401 | ATCC 209774 | April 14, 1998 |
| DNA57039-1402 | ATCC 209777 | April 14, 1998 |
| DNA57033-1403 | ATCC 209905 | May 27, 1998 |
| DNA34353-1428 | ATCC 209855 | May 12, 1998 |
| DNA45417-1432 | ATCC 209910 | May 27, 1998 |
| DNA39523-1192 | ATCC 209424 | October 31, 1997 |
| DNA44205-1285 | ATCC 209720 | March 31, 1998 |
| DNA50911-1288 | ATCC 209714 | March 31, 1998 |
| DNA48329-1290 | ATCC 209785 | April 21, 1998 |
| DNA48306-1291 | ATCC 209911 | May 27, 1998 |
| DNA48336-1309 | ATCC 209669 | March 11, 1998 |
| DNA44184-1319 | ATCC 209704 | March 26, 1998 |
| DNA48314-1320 | ATCC 209702 | March 26, 1998 |
| DNA48333-1321 | ATCC 209701 | March 26, 1998 |
| DNA50920-1325 | ATCC 209700 | March 26, 1998 |
| DNA50988-1326 | ATCC 209814 | April 28, 1998 |
| DNA48331-1329 | ATCC 209715 | March 31, 1998 |
| DNA30867-1335 | ATCC 209807 | April 28, 1998 |
| DNA55737-1345 | ATCC 209753 | April 7, 1998 |
| DNA49829-1346 | ATCC 209749 | April 7, 1998 |
| DNA52196-1348 | ATCC 209748 | April 7, 1998 |
| DNA56965-1356 | ATCC 209842 | May 6, 1998 |
| DNA56405-1357 | ATCC 209849 | May 6, 1998 |
| DNA57530-1375 | ATCC 209880 | May 20, 1998 |
| DNA56439-1376 | ATCC 209864 | May 14, 1998 |
| DNA56409-1377 | ATCC 209882 | May 20, 1998 |
| DNA56112-1379 | ATCC 209883 | May 20, 1998 |
| DNA56045-1380 | ATCC 209865 | May 14, 1998 |
| DNA59294-1381 | ATCC 209866 | May 14, 1998 |
| DNA56433-1406 | ATCC 209857 | May 12, 1998 |
| DNA53912-1457 | ATCC 209870 | May 14, 1998 |
| DNA50921-1458 | ATCC 209859 | May 12, 1998 |
| DNA29101-1122 | ATCC 209653 | March 5, 1998 |
| DNA40021-1154 | ATCC 209389 | October 17, 1997 |
| DNA42663-1154 | ATCC 209386 | October 17, 1997 |
| DNA30943-1-1163-1 | ATCC 209791 | April 21, 1998 |



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|-----------------|-------------|-------------------|
| DNA64907-1163-1 | ATCC 203242 | September 9, 1998 |
| DNA64908-1163-1 | ATCC 203243 | September 9, 1998 |
| DNA39975-1210 | ATCC 209783 | April 21, 1998 |
| DNA43316-1237 | ATCC 209487 | November 21, 1997 |
| DNA55800-1263 | ATCC 209680 | March 17, 1998 |
| DNA94832-2659 | 240-PTA | June 15, 1999 |
| DNA52758-1399 | ATCC 209773 | April 14, 1998 |

The paragraph beginning at page 378, line 33, has been amended as follows:

These deposit were made under the provisions of the Budapest Treaty on the International Recognition of the Deposit of Microorganisms for the Purpose of Patent Procedure and the Regulations there under (Budapest Treaty). This assures maintenance of a viable culture of the deposit for 30 years from the date of deposit. The deposits will be made available by ATCC under the terms of the Budapest Treaty, and subject to an agreement between Genentech, Inc. and ATCC, which assures that all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon the granting of the pertinent U.S. patent, assures permanent and unrestricted availability of the progeny of the culture of the deposit to the public upon issuance of the pertinent U.S. patent or upon laying open to the public of any U.S. or foreign patent application, whichever comes first, and assures availability of the progeny to one determined by the U.S. Commissioner of Patents and Trademarks to be entitled thereto according to 35 USC § 122 and the Commissioner's rules pursuant thereto (including 37 CFR § 1.14 with particular reference to 886 OG 638).